

I claim:

1. A composition capable of inducing apoptosis or necrosis in cancer cells, comprising:

a dithiocarbonyl compound;

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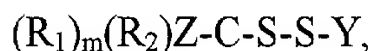
a metal cation;

a modulator of cellular glutathione levels; and

an inhibitor of the phosphorylation of choline.

2. The composition of claim 1, wherein the dithiocarbonyl compound has the formula:

10



wherein m is 0 or 1,

wherein Z is O or N, but if Z is O, then m is 0; and

15

wherein R_1 and R_2 may be independently selected from the group consisting of hydrogen or C1-C24 straight, branched, or cyclic alkyl, alkenyl, aryl, acyl, alkaryl, aralkyl, or alkoxy groups, said groups optionally substituted with ester, ether, halogen, sulfate, hydroxy, or phosphate groups, and wherein R_1 and R_2 may be optionally connected via a bridge comprising $-(CH_2)_n-$, wherein n is 3-8, and wherein said bridge may be optionally substituted independently on

20 any of the carbon atoms with C1-C10 straight, branched, or cyclic alkyl, aryl, aryalkyl, or alkaryl groups, each of said groups optionally substituted with hydroxy, halo, phosphate, sulfate, or sulfonate groups; and

wherein Y is chosen from the group consisting of hydrogen, a pharmaceutically acceptable cation, a physiologically cleavable leaving group, a targeting moiety, or a chemotherapeutic drug.

3. The composition of claim 2, wherein the dithiocarbonyl compound is selected from the group consisting of diethyldithiocarbamate (DEDC); tricyclo-[5.2.1.0^{2,6}]-decyl -9[8]-xanthogenate (D609); tetraethylthiuram disulfide (Disulfuram, ((C₂H₅)₂NCS₂]₂)); and pyrrolidinedithiocarbamate (PDC).
4. The composition of claim 3, wherein the dithiocarbonyl is PDC.
5. The composition of claim 1, wherein the metal cation is selected from the group consisting of Zn²⁺ and Cu²⁺.
6. The composition of claim 1, wherein the metal cation is Zn²⁺.
7. The composition of claim 1, wherein the modulator of cellular glutathione is selected from the group consisting of ethacrynic acid, L-buthionine-S,R-sulfoximine, diethylmaleate, 2-cyclohexene-1-one, and 1-chloro-2,4-dinitrobenzene.
8. The composition of claim 1, wherein the modulator of cellular glutathione is ethacrynic acid.
9. The composition of claim 1, wherein the inhibitor of the phosphorylation of choline is dimethylethanolamine.
10. The composition of claim 1, wherein the dithiocarbonyl compound is PDC in a concentration range of 5-200 μM, wherein the metal cation is Zn²⁺ in a concentration range of 20-500 μM, wherein the modulator of cellular glutathione levels is ethacrynic acid in a concentration range of 10-300 μM, and wherein the inhibitor of the phosphorylation of choline is dimethylethanolamine in a concentration range of 3-40 mM.

11. A method for pre-operative treatment of cancer cells in a tumor prior to surgical removal of the tumor, comprising the steps of:
- providing a composition according to claim 1; and
- causing the composition to contact said cancer cells in the tumor.
- 5 12. The method of claim 11, wherein the step of causing the composition to contact the cancer cells in the tumor is effected by systemic, parenteral, topical, intratumoral, or transdermal administration of the composition.
13. The method of claim 12, wherein the step of causing the composition to contact the majority of cancer cells is by intratumoral administration.
- 10 14. The method of claim 13, wherein the intratumoral administration occurs about 4 hours prior to surgical removal of the tumor.
15. The method of claim 13, wherein the intratumoral administration occurs about 2 hours prior to surgical removal of the tumor.
- 15 16. A method for post-operative treatment of cancer cells in a surgical site remaining after surgical treatment of a primary tumor, comprising:
- providing a composition according to claim 1; and
- causing said composition to contact the surgical site after surgical treatment of said tumor.
- 20 17. The method of claim 16, wherein the step of causing the composition to contact the surgical site is effected by systemic, parenteral, or topical administration of the composition.
18. The method of claim 17, wherein about 50% of the surgical site is exposed to the composition.

19. The method of claim 17, wherein about 90% of the surgical site is exposed to the composition.
20. A method of identifying a therapeutic composition for treating one or more cancers, comprising the steps of:
 - 5 providing the following components for selection into a plurality of test compositions:
 - a dithiocarbonyl compound;
 - a divalent metal ion;
 - a modulator of cellular glutathione; and
 - 10 an inhibitor of the phosphorylation of choline;
 - preparing a plurality of the test compositions, each test composition independently comprising one or more of the components;
 - examining the test compositions to determine if any produce results indicative of biological effect against one or more cancer cell types;
 - 15 and
 - selecting a therapeutic composition to be used in treating one or more cancers based on information comprising the results.
21. The method of claim 20, wherein the biological effect is determined by measuring apoptosis, necrosis, DNA or cellular proliferation rates, or morphological cellular changes.
22. The method of claim 20, wherein the dithiocarbonyl compound is selected from the group consisting of diethyldithiocarbamate (DEDC); tricyclo-[5.2.1.O^{2,6}]-decyl -9[8]-xanthogenate (D609); tetraethylthiuram disulfide (Disulfuram, ((C₂H₅)₂NCS₂-]₂)); and pyrrolidinedithiocarbamate (PDC).

23. The method of claim 20, wherein the metal cation is selected from the group consisting of Zn^{2+} and Cu^{2+} .
24. The method of claim 20, wherein the modulator of cellular glutathione is selected from the group consisting of ethacrynic acid, L-buthionine-S,R-sulfoximine, diethylmaleate, 2-cyclohexene-1-one, and 1-chloro-2,4-dinitrobenzene.
25. The method of claim 20, wherein the inhibitor of the phosphorylation of choline is dimethylethanolamine.
26. A composition capable of inducing apoptosis or necrosis in one or more cancer cells, comprising:
 - a biologically effective amount of a dithiocarbonyl;
 - a biologically effective amount of Zn^{2+} ; and
 - a biologically effective amount of ethacrynic acid.
27. The composition of claim 27, wherein the dithiocarbonyl is PDC.
28. A composition capable of inducing apoptosis or necrosis in one or more cancer cells, comprising:
 - a biologically effective amount of Zn^{2+} ; and
 - a biologically effective amount of ethacrynic acid.
29. A composition capable of inducing apoptosis or necrosis in one or more cancer cells, comprising:
 - a biologically effective amount of ethacrynic acid; and
 - a biologically effective amount of dimethylethanolamine.

30. A composition capable of inducing apoptosis or necrosis in one or more cancer cells, comprising:

a biologically effective amount of a dithiocarbonyl;

a biologically effective amount of ethacrynic acid; and

5 a biologically effective amount of dimethylethanolamine.

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